IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

FOREST LABORATORIES, LLC, FOREST LABORATORIES HOLDINGS, LTD., MERCK KGaA and MERCK PATENT GESELLSCHAFT MIT BESCHRÄNKTER HAFTUNG, Plaintiffs, v. ACCORD HEALTHCARE INC., et al., Defendants.	C.A. No. 15-272 (GMS) CONSOLIDATED

DECLARATION OF MICHAEL THASE, M.D., IN SUPPORT OF
PLAINTIFFS' OPENING CLAIM CONSTRUCTION BRIEF

I, Michael E. Thase, M.D., declare and state:

I. INTRODUCTION

1. I have been retained by Plaintiffs Forest Laboratories, LLC and Forest Laboratories Holdings, Ltd. ("Forest") and Merck KGaA and Merck Patent Gesellschaft mit beschränkter Haftung ("Merck") (collectively, "plaintiffs") in connection with the above-referenced matter as a technical expert on the subject of the diagnosis and treatment of mood disorders, including major depressive disorder.

2. I understand that plaintiffs allege that defendants Accord Healthcare, Inc. ("Accord"), Alembic Global Holding SA, Alembic Pharmaceuticals Inc., and Alembic Pharmaceuticals Ltd. (collectively, "Alembic"), Apotex Inc. and Apotex Corp. (collectively, "Apotex"), Teva Pharmaceuticals USA, Inc. ("Teva"), and InvaGen Pharmaceuticals Inc. ("InvaGen") (collectively, "defendants") have infringed U.S. Patent Nos. 7,834,020 (the "'020

patent"), 8,193,195 (the "'195 patent"), 8,236,804 (the "'804 patent"), and 8,673,921 (the "'921 patent") (collectively, "patents-in-suit"), by filing Abbreviated New Drug Application ("ANDA") Nos. 208209, 208202, 208228, 208212, and 208200, respectively, by seeking FDA approval to make and sell a generic version of Forest's VIIBRYD® product prior to the expiration of the patents-in-suit.

3. I understand that the parties in this case will be asking the Court to define certain terms contained in the patents-in-suit in a process I understand is referred to as "claim construction." I have been asked by plaintiffs to provide, for the benefit of the Court, some technical background on depression and its treatment. I have also been asked to explain how certain terms appearing in the claims of the patents-in-suit would have been understood as of June 2001 by a clinician with experience in treating patients for depression or other conditions identified in the patents-in-suit and evaluating the effects of such treatment.

II. QUALIFICATIONS

4. Since 2007, I have held the position of Professor of Psychiatry at the Perelman School of Medicine of the University of Pennsylvania, and I also serve as the Director of the Perelman School's Mood and Anxiety Disorders Treatment and Research Program. My responsibilities include teaching, seeing patients suffering from various mood disorders, and research; as a senior faculty member, I also have administrative and supervisory responsibilities. My research focuses on the assessment and treatment of mood disorders, including studies of the differential therapeutics of both depression and bipolar affective disorder.

5. I obtained a Bachelor's Degree in psychology from Wright State University in 1975, and an M.D. from the Ohio State University College of Medicine in 1979. My post-graduate training has included an Internship in Medicine and Psychiatry at the Western

Psychiatric Institute and Clinic in Pittsburgh, Pennsylvania in 1979-80; a Residency in General Psychiatry at the Western Psychiatric Institute and Clinic from 1980-1982; and a Postdoctoral Fellowship in Clinical Research at the Western Psychiatric Institute and Clinic from 1982-1984. I also held the position of Chief Resident in Affective Disorders at the Western Psychiatric Institute and Clinic from 1982-1983.

6. From 1983 to 2007, I held various positions in the Department of Psychiatry at the University of Pittsburgh School of Medicine, including Assistant Professor (1983-1987), Associate Professor (1987-1995), and Professor (1995-2007).

7. I taught various classes at the University of Pittsburgh, including: Research Topics in Affective Disorders (1982-1985); Adult Psychopathology (1984-1988); Behavior Therapy Seminar (1983-1990); General Psychiatry II Seminar (1983-1986); Neurosciences Seminars (1985-1988); Introduction to Psychopharmacology (1984-1988); Psychopathology and Normal Development (1987-1982); Neuroscience (1993-1998); Mood Disorders Core Curriculum (1994-2007; Course Director); and Pharmacotherapy of Mood and Anxiety Disorders (1998-2007; Course Director).

8. At the University of Pennsylvania, I give the core lectures on mood disorders to the University's second-year medical students (two classes per year), teach sessions on the diagnosis and treatment of mood disorders to second- and third-year residents (four to six classes per year), and lead a seminar on research strategies and clinical trials methodology (24 classes per year). I also typically supervise two to three residents per year in their advanced electives in mood disorders or clinical research.

9. I am licensed in the fields of medicine and surgery in the Commonwealth of Pennsylvania, and I also hold a specialty certification from the American Board of Psychiatry and Neurology.

10. I have authored or co-authored more than 600 peer-reviewed scientific articles relating to the diagnosis and treatment of mood disorders, including depression. In addition, I have authored or co-authored 16 books and more than 300 reviews, invited published papers, conference proceedings, monographs, book chapters, published abstracts, and other publications in the field.

11. I have lectured at over 300 regional, national, or international symposiums and seminars, most of which focused on the diagnosis and treatment of mood disorders, including depression.

12. I am a member of numerous professional and scientific societies. I am a Distinguished Life Fellow of the American Psychiatric Association, a Founding Fellow of the Academy of Cognitive Therapy, a member of the Board of Directors and President-Elect of the American Society of Clinical Psychopharmacology. I am also a member of the Scientific Advisory Board of the National Depression and Bipolar Support Alliance. I have also been elected to the membership of the American College of Psychiatrists and I am a Fellow of the American College of Neuropsychopharmacology.

13. I have been a member of the editorial boards of numerous publications in the field of psychiatry, including Biological Psychiatry, Journal of Affective Disorders, and International Journal of Clinical Psychopharmacology. In addition, I serve or have served as editor-in-chief of Depressive Disorders: Index and Reviews (1996-1998), Psychopharmacology Bulletin (2002-Current), and Current Psychiatry Reviews (2007-present). I also have served as a grant reviewer

for the National Institute of Mental Health, National Institute of Infectious Disease, and the National Institute on Drug Abuse (1994-2000).

14. Early in my career, I received several honors and awards, including: the Falk Fellowship from the American Psychiatric Association (1981-1983); the Laughlin Fellowship from the American College of Psychiatrists (1983); and the Marie Eldredge Award from the American Psychiatric Association (1984). More recently, I received the Mood Disorders Research Award from the American College of Psychiatrists (2012) and the Alexander Glassman Award from the Department of Psychiatry of the Columbia University College of Physicians and Surgeons (2014).

15. I have received numerous grants for clinical trials relating to depression and other mood disorders in which I served as a Principal or Co-Principal Investigator, including thirteen grants from the National Institute for Mental Health.

16. I also have acted as an advisor to pharmaceutical companies on the development of antidepressants. Since the early 1990s, I have served on the advisory boards for the development of novel antidepressants, including all newly introduced antidepressants dating back to sertraline and bupropion. In this capacity, I advised Forest Laboratories (and its predecessors) on the development of vilazodone. In my role as an advisor, I have consulted with companies at various stages of the development process, starting with evaluation of a compound at the preclinical stage (Phase I) through Phase III and subsequent post-marketing trials. My advice often focuses on issues pertaining to determining dose response relationships, signal detection (*i.e.*, detecting drug versus placebo differences), comparative efficacy, and meta-analyses.

17. In addition to research on antidepressants and other forms of pharmacotherapy, I also have been involved in testing the efficacy of novel forms of herbal or complementary interventions as well as the design and conduct of studies of novel forms of counseling and psychotherapy.

18. Through these experiences, I have developed particular expertise in the treatment of depression and other mood disorders, including evaluation of potential novel and alternative treatments for such disorders.

19. My complete curriculum vitae is attached as Exhibit A.

III. SUMMARY OF OPINIONS

20. I have been asked to explain how the terms "effective amount" ('804 patent, claim 1; '195 patent, claims 1-2; '921 patent, claims 13-14) and "administer"/"administered"/ "administering" ('020 patent, claim 2; '195 patent, claims 1-2; '804 patent, claim 1; '921 patent, claims 10, 12-14) would have been understood by a clinician with knowledge and experience in treating depression and other mood disorders in the early 2000s. In addition, I have been asked to explain the significance, if any, that the preamble beginning with "a method of treating" in certain of the claims of the patents-in-suit would have had to such a clinician. ('020 patent, claim 2; '921 patent, claims 10, 12-14).

21. In connection with the preparation and submission of this declaration, I reviewed the patents-in-suit and their prosecution histories, U.S. Patent No. 5,532,241 (the "'241 patent"), and the parties' proposed claim constructions as set forth in the Joint Claim Construction Chart. Based on my review of the above materials, as well as my background and experience, I have formed the following opinions, which are set forth in more detail below.

22. A clinician with experience treating patients for depression and evaluating the effects of such treatment, including the effects of antidepressants in the early 2000s would understand that the claim term "effective amount" means "amount sufficient to promote a therapeutic effect."

23. A clinician with experience treating patients for depression and evaluating the effects of such treatment, including the effects of antidepressants in the early 2000s would understand that the claim terms "administer," "administered," and "administering" have their plain and ordinary meaning and do not require further definition.

24. A clinician with experience treating patients for depression and evaluating the effects of such treatment, including the effects of antidepressants in the early 2000s would understand that the phrase "a method of treating" in the preamble of claim 2 of the '020 patent, and claims 10 and 12-14 of the '921 patent, is necessary to give meaning to the claim language.

IV. BACKGROUND OF THE INVENTION

25. Mental disorders are the leading cause of disability in the United States for ages 15-44, and the depressive disorders are the most common of these illnesses.[1] Approximately one in six adults will have depression at some point in their lifetime.[2] Depression increases the risk of morbidity and mortality both through suicide as well as co-morbid medical disorders. For example, depression can contribute to or worsen other chronic diseases, including cardiovascular disease, diabetes, asthma, and obesity. In addition, people with depression are more likely to be obese, to smoke, to be physically inactive, and to drink heavily. Depression thus imposes significant personal, social, and economic burdens to patients and society.

[1] T.R. Insel & E.M. Scolnick, *Cure Therapeutics and Strategic Prevention: Raising the Bar for Mental Health Research*, 11 Molecular Psychiatry 1, 11 (2006).
[2] A. Kessler et al., *Lifetime Prevalence and Age-of-Onset Distributions of DSM-IV Disorders in the National Comorbidity Survey Replication*, 62 Archives of Gen. Psychiatry 593-602 (2005).

26. When the application leading to the patents-in-suit was filed (June 2001), almost all of the classes of antidepressant drugs available to treat depression were already available, including tricyclic antidepressants, monoamine oxidase inhibitors, serotonin selective reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), various multi-action medications that primarily work through effects on serotonin receptors (*e.g.*, trazodone, mirtazapine, and nefazodone), and the norepinephrine dopamine reuptake inhibitor bupropion.

27. However, these treatments all suffered from shortcomings. For example, while antidepressants are efficacious in treating the overall population of depressed patients, a large proportion of depressed patients do not respond to current therapies. As many as 50% of patients may not respond to their first medication, with a substantial proportion (30% to 40%) responding when switched to a second regimen.[3] There are no known predictive tools available to guide a doctor's initial choice of therapy for a patient. These limitations existed in the early 2000s, and remain today.

28. Additionally, unwanted side effects of antidepressants are common and overlap with the symptoms of depression itself. Common side effects of antidepressants that emerge early in the course of therapy include nausea, diarrhea, insomnia, and "jitters." Other side effects that emerge after a number of weeks of therapy include sexual dysfunction and weight gain. In particular, sexual dysfunction often undermines treatment by provoking nonadherence to therapy, largely because the time course of sexual dysfunction parallels that of clinical benefit. Thus, patients who are beginning to feel better and who have regained their interest in sex are precisely those who begin to suffer from treatment-emergent sexual dysfunction. Although some medications do not cause sexual dysfunction because they primarily work through other

[3] M.H. Trivedi et al., *Medication Augmentation After the Failure of SSRIs for Depression*, 354 New. Eng. J. Med. 1253-52 (2006).

mechanisms of action (*e.g.*, the NDRI bupropion), these medications typically cannot be used as replacements for patients who have had a full antidepressant response to SSRI therapy because they do not work through serotonin reuptake inhibition. Thus, in June 2001 there was a need for an alternate medication that both inhibited serotonin uptake, yet had a low risk of sexual side effects.

29. As a result of the failure of individual patients to respond to particular antidepressants and the common incidence of side effects, discontinuations and switching of prescriptions are common.[4] The side-effect profile is one of the most frequently cited reasons for patient noncompliance and premature discontinuation of treatment.[5] Thus, any new antidepressant that has effects that differ to some extent from the SSRIs is a tremendously valuable tool for the treatment of depression. This was particularly true in the early 2000s, when there was a great need for medications that offered something more than simply being another SSRI (by far the most frequently prescribed class of antidepressants at that time).

30. The focus on serotonin reuptake inhibition as a primary mechanism of antidepressant action reflects the fact that since the 1970s, depression has been recognized to be attributable, at least in part, to a dysregulation of neurotransmission at central 5-HT synapses. In fact, the SSRIs are thought to initiate antidepressant activity by transiently increasing synaptic 5-HT neurotransmission, which in turn sets in motion other compensatory changes in neurotransmitter signaling within neurons (brain cells). Although this effect may be sufficient for many depressed patients, others do not appear to benefit from SSRI therapy. For other

[4] S.A. Bull, *Discontinuing or Switching Selective Serotonin-Reuptake Inhibitors*. 36 Ann. Pharmacother 578-84 (2002); *see also* M. Olfson et al., *Continuity of Antidepressant Treatment for Adults With Depression in the United States*, 163 Am. J. Psychiatry 101-08 (2006).
[5] Bull, *supra*, at 578-84.

patients, side effects mediated by the serotonin uptake inhibitory effect ultimately can compromise therapy.

31. As a result, researchers believed that combining use of an SSRI with another agent that acts directly upon 5-HT_{1A} receptors could be beneficial in addressing some of these concerns with SSRIs. In the 1980s and early 1990s, researchers attempted to develop or "repurpose" compounds that were 5-HT_{1A} partial agonists, for use as monotherapies or to be given in combination with an SSRI drug. None of these strategies prior to vilazodone were found to reliably improve antidepressant outcomes, although some evidence suggested that adjunctive buspirone therapy has some additive benefit.

32. Vilazodone, the active ingredient in VIIBRYD®, has been shown to possess a novel dual mechanism of action as both a serotonin reuptake inhibitor and 5-HT_{1A} receptor partial agonist. VIIBRYD® is the only antidepressant with these two modes of action, namely, serotonin reuptake inhibition and serotonin 1a partial agonism. Results of preclinical studies suggest that the neurochemical effects of vilazodone differ from what might be expected from combining an SSRI and buspirone in usual doses. Consistent with theoretical predictions of a low rate of sexual side effects, there were few spontaneous reports of anorgasmia or other sexual side effects in the Phase III studies of vilazodone. In fact, the observed rate of sexual side effects with vilazodone was not much different from placebo. Forest Laboratories obtained approval from the FDA for VIIBRYD® for the treatment of major depressive disorder in 2011.

33. Since FDA approval in 2011, VIIBRYD® has proved to be a novel and useful treatment option for doctors and patients because of its dual mechanisms of action and lower side-effect profile compared to other antidepressants.

V. CLAIM CONSTRUCTION

34. The patents-in-suit describe the invention of crystalline forms of vilazodone hydrochloride, pharmaceutical compositions and methods of using the same. Certain of the asserted claims of the patents-in-suit claim methods of treating depressive disorders comprising "administering" the claimed forms of the vilazodone compound to a patient in need of treatment. *See, e.g.*, '804 patent, col. 27, ll. 14-17. Further, certain of the asserted claims claim a method of treatment wherein an "effective amount" of the vilazodone crystalline form is administered to the patient. *See id.*

35. I understand that a patent is read, and the art evaluated, from the perspective of a person of ordinary skill in the art ("POSA") at the time of the relevant priority date (here, June 2001). I also understand that claim terms generally are afforded their plain and ordinary meaning to a POSA, when read in view of the patent specification and prosecution history.

36. I understand that plaintiffs' expert Dr. Bernstein has opined that a person of ordinary skill in the art with respect to the patents-in-suit would have had at least a bachelor's degree in chemistry, pharmaceutical sciences or a related discipline, along with several years of experience working in pharmaceutical solid product development and/or solid state chemistry. I also understand that Dr. Bernstein has opined that a POSA would have access to others with knowledge and experience in treating patients for depression or other conditions identified in the patents-in-suit and evaluating the effects of such treatment. As set forth above, as of the early 2000s, I had substantial experience treating patients for depression and evaluating the effects of such treatment, including the effects of antidepressants.

37. Based on my experience and the materials I reviewed, I set forth my opinions below on how the terms "effective amount" and "administer"/"administered"/"administering,"

and the preamble "method of treating," would have been understood by a clinician experienced in treating patients for depression and evaluating the effects of such treatment in the early 2000s.

A. "Effective amount"

Claim Term	Patent/claim	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"effective amount"	'804 patent, claim 1 '195 patent, claims 1-2 '921 patent, claims 13-14	Amount sufficient to promote a therapeutic effect	An amount of the specified crystalline modification of vilazodone HCl sufficient to produce the desired effect

38. I understand that the parties dispute the meaning of the term "effective amount" as used in the claims of the patents-in-suit. A representative example is claim 1 of the '195 patent, which claims "[a] method of treating a depressive disorder, the method comprising: administering to a patient in need thereof an ***effective amount*** of a compound which is a crystalline hydrochloride salt of [vilazodone], wherein a depressive disorder is treated in the patient." '195 patent, col. 26, ll. 60-65 (emphasis added).

39. In my opinion, a clinician with experience in treating depression as of the early 2000s would have understood the term "effective amount" as used in the claims of the patents-in-suit to mean "amount sufficient to promote a therapeutic effect."

40. "Effective amount" is a common and well-known term in the fields of pharmacology and medicine generally, including in the treatment of depressive disorders. A clinician with experience in treating depression in the early 2000s (and today) would understand that no individual antidepressant agent can be expected to successfully treat depression in all patients. Rather, it is well understood that any given antidepressant may help some patients only a little bit, while helping other patients a lot, and still other patients not at all. Thus, an

experienced clinician in the early 2000s would not expect an "effective amount" to produce a desired effect in all patients. Instead, he or she would understand "effective amount" to mean an amount that promotes or helps to produce the desired effect under controlled circumstances.

41. Based on my review of the patents-in-suit and the file histories, I see no statements that would have led an experienced clinician to have a different understanding of the term "effective amount." For example, the specification describes that "[t]he present invention further provides a method for treating and/or preventing any one or more of the Disorders by administering an effective and/or prophylactic amount of the Products of the Invention to a patient in need thereof." *See, e.g.*, '804 patent, col. 15, ll. 64-67.[6] This language is consistent with the ordinary use of "effective amount" in the field at the time.

42. An experienced clinician in the early 2000s (and today) would understand that no individual antidepressant agent can be expected to successfully treat depression in all patients. Plaintiffs' proposed construction, "amount sufficient to promote a therapeutic effect," is consistent with this reality.

43. This reality is also reflected in the specification for the '241 patent, which I understand is the original compound patent for vilazodone and is incorporated by reference in the patents-in-suit. *See, e.g.,* '804 patent, col. 16, ll. 24-26. The '241 specification describes how "the particular dose for each individual patient depends on a wide variety of factors." *See* '241 patent, col. 8, ll. 48-50. This language reflects the well-known proposition that any given antidepressant may affect individual patients differently.

[6] I understand that the patents-in-suit have identical specifications. Citations to the specification are made to the '804 patent as a representative example, and should be interpreted to include corresponding citations to the '020, '195, and '921 patents.

44. In addition, there are several pharmaceutical products and treatment regimens that include two or more components that work in tandem to promote a therapeutic effect in a patient. For example, there are other psychiatric drugs that are either a combination of stereoisomers or the parent drug is metabolized to include meaningful concentrations of the active metabolite so that two active components are working together in the body (*e.g.*, amitriptyline is metabolized to nortriptyline or venlafaxine is metabolized to desmethylvenlafaxine). The inventors of the patents-in-suit acknowledged this fact by describing that "it may be desirable to employ the specific crystalline forms of the present invention in conjunction with another pharmacologically active agent." *See, e.g.*, '804 patent, col. 16, ll. 10-14. An experienced clinician would not have understood the term "effective amount" to require an amount sufficient to ***produce*** the desired effect, because such an interpretation would seemingly exclude a scenario where a particular drug or treatment regimen has multiple components, none of which alone is sufficient to cause a therapeutic outcome, but together act to generate a desired effect.

45. Therefore, a clinician with experience in treating depression in the early 2000s would have understood the term "effective amount" as used in the claims of the patents-in-suit to mean "amount sufficient to promote a therapeutic effect."

B. "Administer" / "Administered" / "Administering"

Claim Term	Patent/claim	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"administer" "administered" "administering"	'020 patent, claim 2 '195 patent, claims 1-2 '804 patent, claim 1 '921 patent, claims 10, 12-14	Plain meaning/no construction required	Deliver[ed/ing] into the body

46. I understand that the parties dispute the meaning of the terms "administer," "administered," and "administering" as used in the claims of the patents-in-suit. Once again, a representative example is claim 1 of the '195 patent, which claims "[a] method of treating a depressive disorder, the method comprising: ***administering*** to a patient in need thereof an effective amount of a compound which is a crystalline hydrochloride salt of [vilazodone], wherein a depressive disorder is treated in the patient." '195 patent, col. 26, ll. 60-65 (emphasis added).

47. In my opinion, a clinician with experience in treating depression in the early 2000s would have understood that the terms "administer," "administered," and "administering" in the claims of the patents-in-suit have their plain and ordinary meaning and do not require further definition.

48. The terms "administer," "administered," and "administering" are common in the field of medicine generally, including in the treatment of depressive disorders, and are known to refer to the act of providing a patient a drug or treatment for a therapeutic purpose. "Administering" a treatment may encompass a variety of different actions. For example, a doctor can write a prescription for a medication, a pharmacist can dispense a prescribed medication to the patient, or a patient can take a pill orally. An experienced clinician in the early 2000s would have understood all of these acts to be within the scope of "administering."

49. Based on my review of the patents-in-suit and the file histories, I see no statements that would have led an experienced clinician to have a different understanding of the terms "administer," "administered," and "administering." The specification describes that "[t]he present invention further provides a method for treating and/or preventing any one or more of the Disorders by administering an effective and/or prophylactic amount of the Products of the

Invention to a patient in need thereof." *See, e.g.* '804 patent, col. 15, ll. 64-67. Similarly, the '241 patent specification describes the "administration" of substances of the invention without providing further guidance on the meaning of "administer." *See* '241 patent, col. 8, ll. 39-55. This language is consistent with the ordinary use of "administer" in the field at the time.

50. An experienced clinician would not understand "administer" to mean "deliver[ed/ing] into the body." The word "deliver" suggests a narrow focus on inserting the drug into the patient's body, *e.g.*, by actually placing it in the patient's mouth or by intravenous injection. But the term "administer" does not require such a narrow interpretation.

C. "Method of treating" Preamble

Claim Term	Patent/claim	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"A method of treating" preamble	'020 patent, claim 2 '921 patent, claims 10, 12-14	Entire preamble is limiting	"A method of treating" is not limiting

51. I understand that defendants assert that the phrase "a method of treating" in the preambles for claim 2 of the '020 patent, and claims 10 and 12-14 of the '921 patent is not limiting. That is, defendants' position appears to be that only the language "a patient suffering from a depressive disorder, an anxiety disorder, a bipolar disorder, mania, dementia, a substance-related disorder, a sexual dysfunction, an eating disorder, obesity, fibromyalgia, a sleeping disorder, a psychiatric disorder, cerebral infarct, tension, side-effects in the treatment of hypertension, a cerebral disorder, chronic pain, acromegaly, hypogonadism, secondary amenorrhea, premenstrual syndrome, undesired puerperal lactation, or combinations thereof" in those preambles is limiting.

52. I have been informed that a preamble in a patent claim is limiting if it provides essential steps for an invention, or is necessary to give meaning to the language of a patent claim. In my opinion, a clinician with experience in treating depression in the early 2000s would have understood that the entire preamble in each of the above-referenced claims is necessary to give meaning and context to the claim.

53. In treating depression (or any medical condition) in patients, it is critical to understand the intended purpose of the treatment. For example, a patient suffering from a particular disease may be administered medicine for treatment of the underlying disease, prevention of the disease, or to alleviate symptoms of the disease. In the context of depression, treating the underlying disease is expected to result in relief of the characteristic symptoms, including feelings of sadness, hopelessness, insomnia, fatigue, overeating or loss of appetite, headaches or digestive pains. Physicians may prescribe a variety of other types of medications that can alleviate some symptoms, such as insomnia or loss of appetite, but do not necessarily treat the underlying mood disorder.

54. Thus, an experienced clinician would have understood the language "a method of treating" in the context of the claims at issue to make clear that the purpose of administering the product to a patient is treatment of the underlying disorder, rather than, for example, the alleviation of selected symptoms.

55. The specification of the patents-in-suit is consistent with this understanding. The '804 patent describes the invention providing solvates, hydrates, anhydrates, and dihydrochlorides of vilazodone in crystalline modifications "for the treatment ***and prevention***" of various mood disorders. *See* '804 patent, col. 2, l. 39 to col. 3, l. 19 (emphasis added). However, the claims of the patents-in-suit only refer to treatment of such disorders. *See, e.g.*,

’804 patent, col. 27, ll. 14-17. Based on this language, an experienced clinician would further understand that “a method of treating” adds meaning to the claims by making clear they are directed to treatment and not prevention.

56. As a result, a clinician with experience in treating depression in the early 2000s would consider the entire preamble in claim 2 of the ’020 patent, and claims 10 and 12-14 of the ’921 patent necessary to give meaning to the claim language.

57. I reserve the right to amend or supplement my declaration in the event that additional documents and/or information are brought to my attention.

I declare under penalty of perjury that the foregoing is true and correct to the best of my own personal knowledge.

Dated: June 22, 2016

Michael E. Thase, M.D.